REMARKS

I. Status of the Claims

Claims 1, 2, 4-9, 11-15 and 30 will be pending after entry of this amendment. Claim 30 has been amended. Support for the amendment can be found throughout the specification and, for example, in Table 1 on page 83-84, and page 84, line 5. No new matter has been added by this amendment.

Claim 30 is objected to under 37 CFR § 1.75(c). Claims 1, 2, 4-9, 11-15, and 30 are rejected under 35 U.S.C. § 102(b) as being anticipated by Cowsert *et al.* (U.S. Patent No. 6,566,131). Claims 1, 2, 4, 5, 6, 8, 9, 12, 13, 14, and 30 are rejected under 35 U.S.C. § 102(e) as being anticipated by Gimeno *et al.* (U.S. Patent No. 5,955,306).

II. Claim Objection

Claim 30 has been objected to under 37 CFR § 1.75(c), as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Without acceding to the examiner's objection, applicants have amended claim 30 to independent form solely to clarify applicants' claimed invention.

III. The Claims Are Patentable Over the Cited References

Claims 1, 2, 4-9, 11-15, and 30 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Cowsert *et al.* (U.S. Patent No. 6,566,131). In view of the issue date of the patent and applicants' filing date for the instant application, the cited reference, U.S. patent No. 6,566,131, cannot be a 35 U.S.C. § 102(b) reference. Rather, the examiner can only cite U.S. Patent No. 6,566,131 as a potential prior art reference under 35 U.S.C. § 102(e). Therefore, applicants' comments below address the reference as if the examiner meant to cite it as a 35 U.S.C. § 102(e) reference. Applicants traverse the rejection.

Claim 1, and claims dependent therefrom, are directed to an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and inhibits the expression of human vitamin D nuclear receptor. Claim 15 is directed to a method of inhibiting the expression of

vitamin D nuclear receptor in cells or tissues comprising contacting said cells or tissues *in vitro* with an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) so that expression of vitamin D nuclear receptor is inhibited. Claim 30, as amended, is an independent claim directed to an oligonucleotide which specifically hybridizes within a nucleic acid molecule encoding human vitamin D nuclear receptor and inhibits the expression of human vitamin D nuclear receptor, wherein said oligonucleotide comprises a sequence of SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, or SEQ ID NO: 56.

Applicants' claimed invention is novel in view of the Cowsert *et al.* reference since the examiner has failed to provide a rationale or evidence tending to show inherency. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ 2d 1461, 1464 (Bd. Pat. App. & Interfer. 1990); MPEP § 2112.

The examiner has not provided such a basis in fact. The examiner cites the Cowsert *et al.* reference as allegedly disclosing a modified antisense oligonucleotide targeted to Smad6 with the following sequence: 5'- gggtccgttccctcaac-3' (see SEQ ID NO: 25). The examiner further states that the Cowsert *et al.* reference discloses that the antisense oligonucleotide targeted to Smad6 was effective *in vitro* (see Table 1). Contrary to the assertion, the antisense oligonucleotide of the Cowsert *et al.* reference: (see SEQ ID NO: 25), was not effective *in vitro*. In fact, Table 1 and Table 2 show that the antisense oligonucleotide, 5'- gggtccgttccctcaac-3', provides no inhibition ("0% inhibition") of human Smad6 mRNA levels by phosphorothioate oligodeoxynucleotides or by chimeric phosphorothioate oligonucleotides. See U.S. Patent No. 6,566,131, Col. 43, lines 18-59, and Col. 45, lines 1-43. The examiner has not provided any rationale or evidence that the antisense oligonucleotide of the Cowsert et al reference specifically hybridizes to a target sequence within a nucleic acid molecule encoding Smad6. The fact that the antisense

oligonucleotide of the Cowsert *et al.* reference shows 0% inhibition supports the fact that *no specific hybridization* occurs to the target sequence.

MPEP 2112 states that a rejection under 35 U.S.C. §§ 102/103 can be made when the prior art product seems to be identical except that the prior art is silent as to an inherent characteristic. In the instant case, the prior art is not silent with respect to the allegedly inherent characteristic. In fact, the Cowsert *et al.* reference has measured the inherent characteristic, inhibition of Smad16 mRNA levels, and finds 0% inhibition. One must therefore conclude that the characteristic hybridization does not exist for the antisense oligonucleotide to Smad16. Applicants' claimed invention, in part, an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and inhibits the expression of human vitamin D nuclear receptor, is novel in view of the Cowsert *et al.* reference.

For the reasons stated above, the claimed invention is patentable over the Cowsert *et al.* reference. Accordingly, applicants respectfully request that the rejection of claims 1, 2, 4-9, 11-15, and 30 under 35 U.S.C. § 102(e) be withdrawn.

Claims 1, 2, 4, 5, 6, 8, 9, 12, 13, 14, and 30 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Gimeno *et al.* (U.S. Patent No. 5,955,306). Applicants traverse the rejection.

Claim 1, and claims dependent therefrom, are directed to an oligonucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and inhibits the expression of human vitamin D nuclear receptor. Claim 30, as amended, is an independent claim directed to an oligonucleotide which specifically hybridizes within a nucleic acid molecule encoding human vitamin D nuclear receptor and inhibits the expression of human vitamin D nuclear receptor, wherein said oligonucleotide comprises a sequence of SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, or SEQ ID NO: 56.

The examiner has not provided a rationale or evidence tending to show inherency. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. "In relying upon the theory

of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ 2d 1461, 1464 (Bd. Pat. App. & Interfer. 1990); MPEP § 2112.

The examiner has provided no rationale or evidence tending to show inherency. The examiner cites the Gimeno *et al.* reference as allegedly disclosing a modified antisense oligonucleotide targeted to Tub Interact or with the following sequence: 5'-ccctcagcgtcagtcagc-3' (see SEQ ID NO: 27). The examiner further states that the antisense oligonucleotide of the Gimeno *et al.* reference has 89% homology to the reverse complement of nucleotides 1714-1731 of SEQ ID NO:3 of the instant claimed invention. Contrary to these assertions, the examiner has not indicated why the evidence shows that an antisense oligonucleotide targeted to Tub protein, as shown in the Gimeno *et al.* reference, when taken among all oligonucleotides known at the time of filing of the instant application would be sufficient to identify the compound of applicants' claimed invention, *e.g.*, an antisense nucleotide which specifically hybridizes within nucleotides 1710 to 1757 of a nucleic acid molecule encoding human vitamin D nuclear receptor (SEQ ID NO:3) and which inhibits the expression of human vitamin D nuclear receptor. Of the oligonucleotides known to hybridize to target regions at the time of filing of the instant application, no antisense oligonucleotides were known to specifically hybridize within the claimed region of applicants' claimed invention.

For the reasons stated above, the claimed invention is patentable over the Gimeno *et al.* reference. Accordingly, applicants respectfully request that the rejection of claims 1, 2, 4, 5, 6, 8, 9, 12, 13, 14, and 30 under 35 U.S.C. § 102(e) be withdrawn.

IV. Conclusion

In view of the foregoing, the application is now in condition for allowance. The prompt issuance of a formal Notice of Allowance is therefore requested.

If the examiner believes a telephone conference would expedite allowance of this application, please telephone the undersigned at 206-332-1380.

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